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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,232	05/02/2001	Ning Huang	0665-0018.30	5945

22918 7590 04/20/2004

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,232	HUANG ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/12/03; 5/2/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/3/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RCE Acknowledgment

1. The request filed on February 3, 2004 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 09/847,232 is acceptable and a RCE has been established. An action on the RCE follows.

2. Claims 18, and 23-24 are pending and are examined in the present office action.

Specification

3. The specification is objected to because Applicants have not listed the filling dates of the provisional applications from which priority is claimed. Amending the first paragraph of the specification will obviate the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 18, and 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Rejection includes dependent claims.

Claim 18 is indefinite in the recitation "Gt1" and "Reb". The sole designation of a promoter sequence and an amino acid sequence by "Gt1" and "Reb", respectively, is arbitrary and creates ambiguity in the claims. For example, the promoter or amino acid sequence in this application could be designated by some other arbitrary means, or the assignment of said name

could be arbitrarily changed to designate a different promoter or amino acid sequence. If either event occurs, one's ability to determine the metes and bounds of the claim would be impaired. See *In re Hammack*, 427 F .2d 1378, 1382; 166 USPQ 204, 208 (CCPA 1970). Amendment of the claim to refer to a specific SEQ ID NO would obviate this rejection.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 18 and 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of making a modified Gt1 seed-specific promoter responsive to a Reb transcription factor, wherein the sequence of said native Gt1 seed-specific promoter is set forth as SEQ ID NO:26 or wherein the Reb transcription factor is encoded by SEQ ID NO:35.

Applicants disclose the nucleic acid sequence of the Gt1 promoter as set forth in SEQ ID NO:26 and the nucleic acid sequence encoding the Reb transcription factor as set forth in SEQ ID NO:35. Applicants also disclose three upstream activation sequences set forth in SEQ ID NO:36, 37, and 38, to which the Reb transcription factor encoded by SEQ ID NO:35 binds.

Applicants do not identify essential regions of any Gt1 promoter, essential regions of any Reb transcription factor that has the same activity as the protein encoded by SEQ ID NO:35, or essential regions of any upstream activation sequence for the binding of any Reb transcription factor. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences from different plant species that function as a Gt1 promoter; or Applicants fail to describe a representative number polynucleotide sequences from different plant species that encode a Reb transcription factor, or Applicants fail to describe a representative number of upstream activation sequences from different plants to which Reb transcription factors bind. Applicants only describe a single Gt1 promoter of SEQ ID NO:26, a single nucleic acid sequence of SEQ ID NO:35 purportedly encoding a Reb transcription factor and an upstream activation sequence whose sequence is set forth in SEQ ID NO:36 to which the Reb transcription factor

binds. It is noted that SEQ ID NO:36 comprises a sequence in which the 8th base from the left can be either an "A" (SEQ ID NO:37) or a "C" (SEQ ID NO:38). Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the Gt1 promoter, Reb transcription factor or upstream activation sequences to which any Reb transcription factor would bind, it remains unclear what features identify any of these sequences. Since the genus of Gt1 promoter, Reb transcription factors, and upstream activation sequences to which a Reb transcription factor binds has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Applicant's arguments filed 12/12/2003 have been fully considered but they are not persuasive.

Applicants contend that they have fulfilled the written description requirement for the invention because Applicants teach all the necessary steps that are required, i.e., determining the native response sequence for the Reb transcription factor (paragraph bridging pages 5-6), providing a heterologous nucleic acid construct comprising a native monocot Gt1 promoter (paragraph bridging pages 6-7) and inserting a Reb response sequence into a Gt1 promoter (page 7, 1st full paragraph). The Office contends that Applicants have not fulfilled the written description requirement for a method of making any modified Gt1 seed specific promoter responsive to any Reb transcription factor. Applicants have not taught the genus of Gt1 promoters, the genus of Reb transcription factors or the genus of upstream activation sequences to which any Reb transcription factor will bind. Applicants are only in possession of a Gt1

promoter of SEQ ID NO:26, a Reb transcription factor encoded by SEQ ID NO:35 and an upstream activation sequence of SEQ ID NO:36 inserted in a particular location within the Gt1 promoter. Applicants have not fulfilled the written description requirement for the genus of Gt1 promoters, the genus of Reb transcription factors or the genus of upstream activation sequences.

Scope of Enablement

6. Claims 18 and 23-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a rice glutelin 1 (Gt1) promoter of SEQ ID NO:26 in which a 98 bp *Oryza sativa* bZIP (Reb) upstream activation sequence (UAS) fragment containing three copies of GCCACGT(C/A)AG whose sequence is set forth in SEQ ID NO:36 was inserted at position -630 bp distal to the TATA box of said Gt1 promoter (page 31, lines 13-19), operably linked to any encoding nucleic acid sequence and co-transformed with a nucleic acid sequence of SEQ ID NO:35 which encodes a Reb transcription factor, to increase expression of said encoding nucleic acid sequence compared to a plant not transformed with the Reb transcription factor (page 31, lines 20-25), does not reasonably provide enablement for claims broadly drawn to a method of making any Gt1 seed-specific promoter responsive to any Reb transcription factor comprising determining the native response sequence for any Reb transcription factor, and inserting said responsive sequence into any Gt1 promoter in any location. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a method of making a modified Gt1 seed-specific promoter responsive to any Reb transcription factor comprising determining the native response sequence for any Reb transcription factor and inserting said sequence anywhere in any Gt1 seed-specific promoter wherein the binding of any Reb transcription factor to said response sequence results in an increase in the expression of a gene under the control of said Gt1 seed specific promoter, wherein the sequence of said Gt1 seed-specific promoter is set forth as SEQ ID NO:26 or wherein the nucleic acid sequence that encodes said Reb transcription factor is set forth as SEQ ID NO:35.

Applicants have isolated a sequence from the rice globulin (Glb) promoter to which binds the Reb protein of SEQ ID NO:35. Applicants have disclosed this sequence which contains the motifs GCCACGTCAG and GCCACGTAAG (GCCACGT(A/C)AG) (page 31, lines 26-36) and have inserted this sequence into position -630 bp distal to the TATA box of said Gt1 promoter (page 31, lines 13-19).

Applicants have only taught the Gt1 seed-specific promoter of SEQ ID NO:26, the Reb transcription factor encoded by SEQ ID NO:35, and the upstream activation sequence of SEQ ID NO:36 to which said Reb transcription factor binds. Applicants are not enabled for any Gt1 seed-specific promoter, any Reb transcription factor or any upstream activation sequence to which any Reb transcription factor binds, given that Applicants have not disclosed how one skilled in the art can identify and/or isolate the genus of Gt1 promoters, the genus of Reb transcription factors, and the genus of upstream activation sequences. One skilled in the art would not know how to identify all Gt1 seed-specific promoters, Reb transcription factors or upstream activation sequences. Furthermore, Applicants claims are drawn to inserting the upstream activation sequence anywhere within the Gt1 promoter but Applicants have only taught one location.

Applicants have described a transactivation-like system which utilizes a transcription factor that acts in trans to bind to a cis-acting element that has been incorporated into a promoter. In the present application, the promoter is any seed-specific promoter. The state-of-the-art teaches transactivation systems produce unpredictable results. Schwechheimer et al (2000, Funct Intergr Genomics 1:35-43) teach transactivation systems have inherent problems which leads to unpredictability within the system. They report "Many genes encoding transcriptional activators are differentially expressed or activated in different tissues at different stages of organismal development or in response to environmental stimuli" (page 35, right column, 1st paragraph). In addition, "numerous transcriptional activators vary in their strength and possibly in some cases also in their tissue-specific activity" (page 41, left column, 2nd paragraph). They also report that target gene silencing is a problem that can occur if there is a high concentration of transcription

factors within the nucleus (page 41, right column, 1st paragraph) or that the upstream activation sequences become methylated. Schwechheimer et al state "It has been postulated that the GAL4-promoter binding sites may be methylated and that methylation interferes with promoter activity" (page 41, right column, 1st paragraph). Schwechheimer et al also teach that not all promoters confer the same level of expression in all plant system (page 36, left column, 2nd paragraph).

Applicants have claimed a method of making a seed-specific promoter, comprising inserting a response sequence anywhere within the seed-specific promoter. But, inserting it anywhere will lead to deletions, substitutions or rearrangements within the original seed-specific promoter which cannot be expected to maintain the original promoter or enhancer activity, or to have any activity. Izawa et al (1993, J. Mol. Biol. 230 :1131-1144) teach the nucleotides flanking the G-box (CACGTC) and C-box (GACGTC) hexameric cores were shown to affect protein binding activity and specificity of bZIP transcription factors (of which Reb is a member) (page 1132, bottom of right column; page 1134, bottom of left column). Hao, et al (1998, The J. of Biological Chemistry 273 (41): 26857-26861) investigated the binding activities of ethylene-responsive element-binding proteins (EREBP) to their cis-element GCC box (AGCCGCC). Creating base-pair substitutions within the GCC box modulates binding specificity, implying that different positions within the GCC box are important for differential binding by different EREBP's, in particular, substituting T's for the two G's eliminates binding completely (*supra*, pages 26857, abstract and 26860, left column, 2nd paragraph). Given the rationale set forth above, Applicants are not enabled for a method of making a modified Gt1 seed-specific promoter

comprising inserting an upstream activation sequence to which any Reb transcription factor binds anywhere within the Gt1 seed-specific promoter.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill to make a modified Gt1 seed-specific promoter comprising isolating other Reb transcription factors by using non-disclosed regions of a nucleic acid encoding the Reb transcription factor of SEQ ID NO:35 as probes or by designing primers to non-disclosed regions of a nucleic acid encoding the Reb transcription factor of SEQ ID NO:35, and then to identify and isolate upstream activation sequences to which the Reb transcription factor binds; isolating other Gt1 seed-specific promoters using non-disclosed fragments of SEQ ID NO:26, or by designing primers to undisclosed regions of SEQ ID NO:26 and isolating or amplifying fragments, subcloning the putative upstream activation sequences into all possible locations in the Gt1 promoter so as to make a modified Gt1 promoter that is operably linked to a nucleic acid encoding a protein; transforming plants with the modified promoter sequence operably linked to a nucleic acid encoding a protein and also transforming the plant with the putative Reb transcription factor, in order to identify those plants, if any, that exhibit an increased expression of the encoding nucleic acid compared to a plant not transformed with the modified Gt1 seed-specific promoter.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Applicant's arguments filed 12/12/2003 have been fully considered but they are not persuasive.

Applicants contend that the enablement requirement is fulfilled for the claimed invention, i.e., undue experimentation is not required to make and use the claimed invention. Applicants contend that all the necessary guidance is provided in the specification for making the claimed invention without undue experimentation (pages 9-12). The Office contends that Applicants have fulfilled the enablement requirement for claims drawn to a method of making a modified rice glutelin 1 (Gt1) promoter of SEQ ID NO:26 in which a 98 bp *Oryza sativa* bZIP (Reb) upstream activation sequence (UAS) fragment containing three copies of GCCACGT(C/A)AG whose sequence is set forth in SEQ ID NO:36 was inserted at position -630 bp distal to the TATA box of said Gt1 promoter (page 31, lines 13-19), operably linked to any encoding nucleic acid sequence and co-transformed with a nucleic acid sequence of SEQ ID NO:35 which encodes a Reb transcription factor, to increase expression of said encoding nucleic acid sequence compared to a plant not transformed with the Reb transcription factor (page 31, lines 20-25). Applicants are not enabled for the broadly claimed invention for the reasons given above.

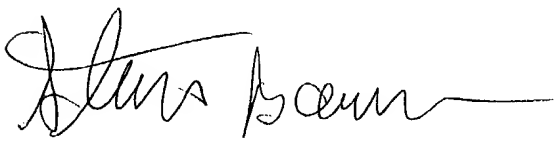
7. Claims 18, 23 and 24 are free of the prior art, given the failure of the prior art to teach or reasonably suggest a method of making a modified Gt1 seed-specific promoter of SEQ ID NO:26 responsive to a Reb transcription factor encoded by SEQ ID NO:35, comprising inserting a Reb response sequence comprising three copies of SEQ ID NO:36 into the Gt1 promoter sequence.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
April 15, 2004